

CLAIMS

1. A method of early diagnosing chronic rejection (CR) in a transplanted subject comprising
 - a) taking as a baseline value the level of mRNA expression corresponding to or protein encoded by at least one gene, the gene originating from a specific allograft tissue biopsy of a transplanted subject who is known not to develop CR;
 - b) detecting a level of mRNA expression corresponding to or protein encoded by the at least one gene identified in a) in an allograft tissue biopsy of the same tissue type as in a) obtained from a patient within the first year post-transplantation; and
 - c) comparing the first value with the second value, wherein a first value lower or higher than the second value predicts that the transplanted subject is at risk of developing CR.
2. A method according to claim 1, wherein the baseline value a) is obtained by detecting a level of mRNA expression corresponding to or protein encoded by at least one gene in an allograft tissue biopsy obtained from the donor at the day of transplantation.
3. A method for monitoring CR in a transplanted subject at risk of developing CR comprising
 - a) obtaining a pre-administration sample from a transplanted subject prior to administration of a CR inhibiting agent,
 - b) detecting the level of expression of mRNA corresponding to or protein encoded by the at least one gene in the pre-administration sample,
 - c) obtaining one or more post-administration samples from the transplanted patient,
 - d) detecting the level of expression of mRNA corresponding to or protein encoded by the at least one gene in the post-administration sample or samples,
 - e) comparing the level of expression of mRNA or protein encoded by the at least one gene in the pre-administration sample with the level of expression of mRNA or protein encoded by the at least one gene in the post-administration sample or samples, and
 - f) adjusting the agent accordingly.
4. A method for preventing, inhibiting, reducing or treating CR in a transplanted subject in need of such treatment comprising administering to the subject a compound that modulates the synthesis, expression or activity of one or more genes or gene products as identified in claim 1 or 2, so that at least one symptom of CR is ameliorated.

5. A method for identifying agents for use in the prevention, inhibition, reduction or treatment of CR comprising monitoring the level of mRNA expression of one or more genes or gene products as identified in claim 1 or 2.
6. A method according to claim 1, 3 or 4, wherein the transplanted subject is a kidney transplanted subject.
7. A method according to claim 5 or 6, wherein the genes are selected from the group of genes as identified in Table 1 and/or 2 and/or 3.
8. A method according to claim 1, 3, 4 or 5, wherein the level of expression of the gene expression is assessed by detecting the presence of a protein corresponding to the gene expression product.
9. A method according to claim 8, wherein the presence of the protein is detected using a reagent which specifically binds to the protein.
10. A method according to claim 1, 3, 4 or 5, wherein the level of mRNA expression of one or more genes is detected by techniques selected from the group consisting of Northern blot analysis, reverse transcription PCR and real time quantitative PCR.
11. A method according to claim 1, 3, 4 or 5 wherein the level of mRNA expression of a set of genes is detected.
12. Use of a gene or an expression product of a gene as listed in Table 1, 2 or 3 as an early biomarker for chronic transplant rejection.
13. Use of a gene or an expression product of a gene as listed in Table 1, 2 or 3, excluding FAS gene missing exon 4, retinoblastoma binding protein 7, prohibitin and connective tissue growth factor, as a biomarker for chronic transplant rejection.
14. Use of a compound which modulates the synthesis, expression of activity of one or more genes as identified in Table 1, 2 or 3, or an expression product thereof, for the preparation of a medicament for prevention or treatment of CR in a transplanted subject.